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10/533,950	05/04/2005	Andre Roget	271326US0PCT	9633

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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
HAQ, SHAFIQUL	

ART UNIT	PAPER NUMBER
1641	

NOTIFICATION DATE	DELIVERY MODE
04/21/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/533,950	ROGET ET AL.	
	Examiner	Art Unit	
	SHAFIQUL HAQ	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 10-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 10-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendments and arguments filed 12/28/07 is acknowledged and entered.

2. Claims 1-6 and 10-23 are pending.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-3, 6, 10-23 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Biosensors and Bioelectronics 1998) in view of Domb (US 2006/0013850A1) and Guedon et al (Anal Chem. 2000).

Livache et al disclose a method of immobilization of biological material (e.g. DNA, peptides, protein) (lines 14-15, right column of page 629) to a conductive support (e.g biochip) by means of a pyrrole polymer (see abstract and introduction). The method comprises coupling biomolecules to pyrrole monomer and mixing solutions of pyrrole monomer and biomolecules bearing a pyrrole group (DNA or peptide) to obtain an electropolymerization solution and elctropolymerization to obtain a film of copolymer on conductive medium (see sections 2.1. and 2.3. of page 630). The pyrrole copolymerization process allows the preparation of addressed polypyrrole-DNA/protein on blocks of biosensor array (see section 3.; fig.5 and lines

6-9, right column of page 633). Examples of immobilization of proteins (e.g ACTH hormone) and DNA (Fig. 5; Fig.6 and section 3.4.) are also disclosed.

Livache et al. disclose pyrrole peptides/proteins but, however, do not disclose pyrrole monomers coupled to peptides/proteins using activated pyrrole (i.e. pyrrole monomers activated with coupling groups).

Domb (US 2006/0013850 A1) discloses coating of electropolymerized pyrrole polymers to conductive support (paragraphs [0019], [0027]). Domb also discloses that the electropolymerized polymer can have a second monomer bearing a reactive group/ functional group (paragraphs [0032], [0044], [0051] and [0055]) for binding to bioactive agents such as proteins, enzymes, nucleic acids (paragraph [0024], [0182], [0243], [0244]). Domb further discloses that activated pyrrole monomers {(e.g. N-alkyl pyrrole derivatives possessing functional groups such as carboxylic acid and derivatives thereof (e.g. acyl halide, ester), amine, hydroxyl, vinyl, acetylene and thiol} can be used for binding bioactive agents (paragraphs [0209], **[0396]** and example 1, especially scheme 1, scheme 2 and PPA-NHS). Domb et al. further discloses conditions for attachment of bioactive agent such as peptides and proteins to activated pyrrole monomers (paragraph [0396] and [0397]).

Therefore, given the above disclosure the pyrrole monomers can be coupled to proteins efficiently through activated pyrroles (Domb) (i.e. pyrrole having a reactive group), it would be obvious to one of ordinary skill in the art at the time the invention was made, to use pyrrole monomer coupled to proteins as taught by Domb in the

electropolymerizing mixture of Livache et al. for immobilizing peptides/proteins to conductive support, with a reasonable expectation of success.

As for amount of current and syntyhesis time, Livache et al disclose different thickness (from 2 to 80 nm approximately) which were obtained by applying an amount of current from 10 to 400uC/mm^2 (section 3.2., 3.4. and Fig. 4) but do not suggest electopolymerization being carried out with a charge of less that 50uC/mm^2, for a synthesis time of less than 1000ms to obtain a film of copolymer thickness to about 10nm.

Guedon et al in a polypyrrole-based DNA sensor disclose six different thickness of polypyrroly-ODN spots made by performing the synthesis for 250ms to 1000ms leading to 9-14 nm thick films (page 6007, left column, left column, lines 3-12). The film synthesis is very fast taking about 500ms to spot an 11 nm thick film by a 2-V electrochemical pulse (page 6004, lines 30-31 of left column and page 6005, left column, lines 7-8). Goedon also discloses that for optimal hybridization signal, optimal thickness of the spot was found to be close to 11 nm (see abstract; page 6007, lines 1-1-26 of left column and Fig. 6).

Therefore, given the above fact that a film of pyrrole containing copolymer having a thickness close to 11 nm is desirable for optimal hybridization signal (Guedon et al), it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to introduce polymer film thickness close to 11nm (i.e 10nm) in the method of Livache et al, with the expectation of enhancing detection signal and to produce a thickness close to nm within 250ms to 1000ms (Goedon)

with a electrode of 50um x 50um, an electric current of less that 50uC/mm^2 is obvious as described above. Optimal thickness of 11 mm is disclosed by Guedon but, however, the optimal thickness for a particular application can be varied by routine optimization by the variation of electric current.

Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the .general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454,456, 105 USPQ 233,235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 .("The normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages."); In re Hoeschele, 406 F.2d 1403, 160 USPQ 809 (CCPA 1969) (Claimed elastomeric polyurethanes which fell within the broad scope of the references were held to be unpatentable thereover because, among other reasons, there was no evidence of the criticality of the claimed ranges of molecular weight or molar proportions.)

As for location of the conductive support to biosensor device and use of the biosensor device for different purposes (claims 17-21), Livache's conductive support is meant to be used as biosensors and the location and use of the conductive support constitute obvious variations in parameters which are routinely modified in the art and which have not been described as critical to the practice of the invention.

5. Claims 4 is again rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Biosensors and Bioelectronics 1998) in view of Domb (US 2006/0013850A1) and Guedon et al (Anal Chem. 2000) as applied to claims 1-3 and 6-9 above, and further in view of Caillat et al (US 6,803,228).

Livache et al in view of Domb and Guedon et al disclose a method of immobilization of proteins to a conductive support (e.g biochip) by means of a pyrrole polymer as describes above, but the references fail to disclose pyrrole functionalized with maleimide for coupling to protein.

Caillat et al disclose pyrrole polymer functionalized with N-hydroxysuccinimide and maleimide for coupling to biomolecules (see 3rd compound from top in column 4 and lines 63-67).

Therefore, given the fact that functionalization of pyrrole with N-hydroxysuccinimide or maleimide is know and common in the art (Caillat et al), it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to functionalize pyrrole monomer with maleimide in the method of Livache et al, with the expectation of producing similarly useful conductive support containg polymer of pyrrole coupled with protein.

6. Claims 1-3, 6, 10-21 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Biosensors and Bioelectronics 1998), Domb, Guedon et al (Anal Chem. 2000) and Caillat et al (US 6,803,228) as applied to claim 4 in the preceding paragraph, and further in view of Bianchi et al (US 2003/0207400 A1).

The above paragraph 6 describes a method of immobilization of biological material (e.g. DNA or peptide) to a conductive support (e.g biochip) by means of a pyrrole polymer and also disclose pyrrole functionalized with succinimide or

maleimide for coupling to protein but the references do not disclose the linkers use to functionalize pyrrole with maleimide as claimed in claim 5.

Bianchi et al disclose different linkers (see scheme 15, 20 and 28) to functionize pyrrole with thiol, maleimide or amino groups and the linkers are either the same as or homologs of the linkers of the instant claim 5.

Therefore, given the fact that functionalization of pyrrole with N-hydroxysuccinimide or maleimide is know and common in the art (Caillat et al) and linkers of different chain length can be employed (Banchi et al), it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to functionalize pyrrole monomer with N-hydroxysuccinimide or maleimide using the linker of Banchi et al, in the method of Livache et al, with the expectation of producing similarly useful conductive support containg polymer of pyrrole coupled with protein. Furthermore, the chain length of the linker do not appear to be critical to the practice of the invention as different chain length linkers can be used and would be obvious to one of ordinary skill in the art unless unexpected results are presented for the linkers as disclosed.

7. Claims 1-3 and 6-9 are again rejected under 35 U.S.C. 103(a) as being unpatentable over Livache et al (Analytical Biochemistry 1998) in view of Livache et al (Biosensors and Bioelectronics 1998) and Guedon et al (Anal Chem. 2000).

Livache et al (Analytical Biochemistry) disclose a method of immobilization of oligonucleotide (ODN) to a conductive support (e.g DNA chip) electrochemically by means of a pyrrole polymer (see abstract and lines 6-10 of right column of page

188). The method comprises coupling oligonucleotide to pyrrole monomer and mixing solutions of pyrrole monomer and oligonucleotide bearing a pyrrole group to obtain an electropolymerization solution and elctrooxidization to obtain a film of copolymer on conductive medium (Lines 6-10 of right column of page 188 and Fig.1 of page 189). The pyrrole copolymerization process allows the preparation of addressed ODN-pyrrole on blocks of biosensor array so that different oligonucleotides can be immobilized to different blocks of biochip (see B of Fig.1). Livache et al disclose (Analytical Biochemistry) different thickness of polypyrrole film deposited on the surface (page 192). Synthesis of the film is stopped when the current applied reaches 125, 160, 200, 250 and 375 nC, values which correspond to respectively- for electrodes measuring 50um x 50um – to 50, 64, 80, 100 and 150 uC/mm^2 and to a thickness of 10, 16, 20 and 30 nm.

Livache et al (Analytical Biochemistry) do not disclose coupling proteins to pyrrole monomer but suggest copolymerization of many biological molecules (which includes DNA, proteins etc) for immobilization by means of pyrrole polymerization (lines 42-44 of left column of page 194). Livache et al (Analytical Biochemistry) do not suggest electopolymerization being carried out with a charge of less that 50uC/mm^2, for a synthesis time of less than 1000ms to obtain a film of copolymer thickness to about 10nm, although a range of thickness and a range of currents applied are disclosed.

Livache et al (Biosensors and Bioelectronics 1998) as described in above paragraph 11 disclose of immobilization of peptide to a conductive support by means of a pyrrole polymer wherein protein is coupled to pyrrole monomer.

Guedon et al in a polypyrrole-based DNA sensor disclose six different thickness of polypyrroly-ODN spots made by performing the synthesis for 250ms to 1000ms leading to 9-14 nm thick films (page 6007, left column, left column, lines 3-12). The film synthesis is very fast taking about 500ms to spot an 11 nm thick film by a 2-V electrochemical pulse (page 6004, lines 30-31 of left column and page 6005, left column, lines 7-8). Goedon also discloses that for optimal hybridization signal, optimal thickness of the spot was found to be close to 11 nm (see abstract; page 6007, lines 1-1-26 of left column and Fig. 6).

Therefore, given the above fact that a film of pyrrole containing copolymer having a thickness close to 11 nm is desirable for optimal hybridization signal (Guedon et al), it would have been prima facie obvious to one of ordinary skill in the art at the time of the instant invention to include proteins for immobilization as taught by Livache et al (Biosensors and Bioelectronics 1998) and introduce polymer film thickness close to 11nm (i.e 10nm) (as suggested by Guedon et al) in the method of Livache et al (Analytical Biochemistry), with the expectation of enhancing detection signal and to produce a thickness close to 11nm (i.e. 10nm) within 250ms to 1000ms (Goedon) with a electrode of 50um x 50um, an electric current of less that 50uC/mm^2 is obvious as described above.

As for, coupling of pyrrole monomers to proteins, Livache et al. disclose pyrrole peptides/proteins but, however, do not disclose pyrrole monomers coupled to peptides/proteins using activated pyrrole (i.e. pyrrole monomers activated with coupling groups).

Domb (US 2006/0013850 A1) discloses coating of electropolymerized pyrrole polymers to conductive support (paragraphs [0019], [0027]). Domb also discloses that the electropolymerized polymer can have a second monomer bearing a reactive group/ functional group (paragraphs [0032], [0044], [0051] and [0055]) for binding to bioactive agents such as proteins, enzymes, nucleic acids (paragraph [0024], [0182], [0243], [0244]). Domb further discloses that activated pyrrole monomers {(e.g. N-alkyl pyrrole derivatives possessing functional groups such as carboxylic acid and derivatives thereof (e.g. acyl halide, ester), amine, hydroxyl, vinyl, acetylene and thiol} can be used for binding bioactive agents (paragraphs [0209], **[0396]** and example 1, especially scheme 1, scheme 2 and PPA-NHS). Domb et al. further discloses conditions for attachment of bioactive agent such as peptides and proteins to activated pyrrole monomers (paragraph [0396] and [0397]).

Therefore, given the above disclosure the pyrrole monomers can be coupled to proteins efficiently through activated pyrroles (Domb) (i.e. pyrrole having a reactive group), it would be obvious to one of ordinary skill in the art at the time the invention was made, to use pyrrole monomer coupled to proteins as taught by Domb in the electropolymerizing mixture of Livache et al. for immobilizing peptides/proteins to conductive support, with a reasonable expectation of success.

As for location of the conductive support to biosensor device and use of the biosensor device for different purposes (claims 17-21), Livache's conductive support is meant to be used as biosensors and the location and use of the conductive support constitute obvious variations in parameters which are routinely modified in the art and which have not been described as critical to the practice of the invention.

Response to Applicant's argument

8. Applicant's arguments filed 12/28/07 have been fully considered but are not found convincing for the following reasons:

Applicants argued that the Domb priority document PCT '806 does not disclose the coupling of an activated pyrrole to a protein to from a protein-pyrrole coupling compound in which the coupling implements a covalent bond between the activated pyrrole and the protein as required by the present invention. Applicants cited page 21, Example 3 and claims 21-22 of PCT '806 to argue that the priority document refers to polymeric coating containing oxidized polypyrrole derivatives with anionic peptides and proteins. Applicants' argument have not been found convincing because PCT '806 clearly discloses activation of pyrrole with functional group for coupling with peptides through covalent linkages. See example 2 of page 17 of the PCT '806, where carboxy and amino containing pyrrole derivatives are disclosed and disclose activativation with reactive derivatives such as acid chloride, anhydride, N-succinimide or activation with DCC for covalent conjugation. Lines 23-28 of page 18, wherein the PCT '806 discloses activation of pyrrole and coupling of the

activated pyrrole covalently to heparin activation of pyrrole. See also lines 1-6 or page 19, which discloses carbodimide activation of pyrrole for conjugation to bioactive molecules and peptides. Further, Page 18, lines 26-28 discloses carbodiimide mediated covalent coupling of aminoproply pyrrole or carboxyethyl pyrrole to protenic molecules. Therefore, coupling of pyrrole to a protein in PCT '807 is not a new matter for Domb (US 2006/0013850).

Wit regard to optimal thickness, see the discussion in paragraph 4 of this office action.

Conclusion

9. **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SHAFIQUL HAQ whose telephone number is (571)272-6103. The examiner can normally be reached on 7:30AM-4:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Shafiqul Haq/
Examiner, Art Unit 1641

/Long V Le/
Supervisory Patent Examiner, Art Unit 1641